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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,644	12/11/2000	Jean Gariepy	MMC.P-001	7797

21121 7590 12/03/2004

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EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/601,644	GARIEPY ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,24,25 and 27-42* is/are pending in the application.

4a) Of the above claim(s) *17,18,20,24,25 and 27-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/1/01, 7/23/01, 11/20/00.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Communication & Notice to Comply

DETAILED ACTION

1. Claims 1-18, 20, 24, 25, 27-42 are pending. Claims 17, 18, 20, 24, 25, 27-42 are withdrawn from consideration. Claims 1-16 are examined.

Election/Restrictions

2. Claims 17-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species and inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/11/04.

3. Applicant's election with traverse of Group I, and the species of Shiga like toxin and tumor cells, in the reply filed on 10/11/04, is acknowledged. The traversal is on the ground(s) that there is no lack of unity for claims 1-42, because the new amendment of claim 1, filed 10/12/04, overcomes the finding of anticipation by the references of Jackson et al., Perera et al. and Smedley et al., as set forth in the restriction requirement, mailed 8/10/04. This is not found persuasive because the previously cited reference of Jackson et al., and the newly cited reference of Tyrrell et al., anticipate the invention as claimed in newly amended claim 1. Therefore, the examiner respectfully submits that there continues to be no special technical feature linking the claims. Please see the below rejections under 35 USC 102 (b). In the interest of compact prosecution, and because the grouping of the claims is still proper for the claims as amended, the amended claims of Group I are examined, herein.

The requirement is still deemed proper and is therefore made FINAL.

Nucleotide and Amino Acid Sequence Disclosures

4. The instant specification, at p. 18, Table 1, p. 21, Table 2, p. 23, Table 3, appears to disclose nucleotide and amino acid sequences that are not referred to by a sequence identifier or listed on the SEQ ID Listing or the Computer Readable Form. Applicant must submit a new SEQ ID Listing identifying all nucleotide and amino acid sequences by Sequence Identifier; submit a new CRF copy of the new SEQ ID Listing; and submit a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d), (please see also attached letter and Notice to Comply).

Specification

5. The instant specification is objected to and must be amended to identify all nucleotide and amino acid sequences by SEQ ID No. In particular, the nucleotide and amino acid sequences in the instant specification at p. 18, Table 1, p. 21, Table 2, p. 23, Table 3, appear to not be so identified. Applicant is requested to assist in correcting any other incidence of non-complying sequence disclosures in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the language "wild type protein said mutant protein" in line 2, which appears to lack a comma and probably should read as "wild type protein, said mutant protein". Claim 6 recites the language "(D) incorporated said cassette", which appears to be of the wrong tense and probable should read as "(D) incorporating said cassette". Claim 8 appears to recite an improper Markush group; and might read, for example, "is selected from **the** group consisting of prokaryotic proteins, eukaryotic protein and protein fusion constructs capable of blocking protein synthesis." Claim 9 contains a typographical error and should read "consisting of" in line 2. Claim 9 appears to recite an improper Markush group; and might read, for example, "is selected from **the** group consisting of Shiga toxin, Shiga-like toxins, ricin, abrin, gelonin, crotin, pokeweed antiviral protein, saporin, momordin, modeccin, sarcin, diphtheria toxin and Pseudomonas aeruginosa exotoxin A."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-3, 5, 8-13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Jackson et al., J. of Bacteriology, Feb. 1990, Vol. 172, No. 2, pp. 653-658, (previously cited with the Requirement for Restriction/Election, mailed 8/10/04).

The claims are drawn to a method for making cytotoxic mutant proteins having different receptor-binding specificity than the wild type protein, comprising: (A) selecting

a heteromeric protein toxin having a toxic domain subunit and a binding domain subunit; (B) incorporating mutations into DNA encoding the binding domain subunit to produce variants of the toxin; (C) generating a library of microorganism clones producing variant forms of toxin; (D) screening the variants by isolating clones producing said variant forms, treating cells with the variant toxins, and selecting cytotoxic mutant proteins that inhibit or kill the cells to a greater extent than the wild-type cytotoxic protein; and (E) making copies of the selected mutant proteins, and variations thereof.

Jackson et al., throughout the publication, and especially at the abstract, p. 653, para 1-2, and p. 655, Fig. 1, teach the verotoxin or Shiga-like toxin) family is a group of subunit toxins, with an A subunit and a B binding subunit, and the site-directed mutagenesis of the B subunit; at p. 653, para 3-p. 654, para 1, and p. 655, Table I, generating a library of E. coli that produced variant forms of the toxin; at p. 654, para 5-p. p. 655, para 2, teach extracellular supernatants and cell-associated fractions (of the microorganism E. coli library) that are used for microcytotoxicity assays using Vero cells and HeLa (tumor) cells and glycolipid receptor binding ELISA assays; and at para 5-p. 655, para 1, p. 656, para 4, and Table 3, teach amber termination mutations in the Shiga toxin B unit, wherein the double suppressor host LE392 expresses 2 to 3 orders of magnitude more cytotoxicity than the single suppressor host HB101 (Table 3).

8. Claims 1-3, 5, 8-13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Tyrrell et al., Proc. Natl. Acad. Sci. USA, vol. 89, pp. 524-528, Jan 1992 (IDS filed 11/20/2000).

The claims are drawn to a method for making cytotoxic mutant proteins having different receptor-binding specificity than the wild type protein, comprising: (A) selecting a heteromeric protein toxin having a toxic domain subunit and a binding domain subunit; (B) incorporating mutations into DNA encoding the binding domain subunit to produce variants of the toxin; (C) generating a library of microorganism clones producing variant forms of toxin; (D) screening the variants by isolating clones producing said variant forms, treating cells with the variant toxins, and selecting cytotoxic mutant proteins that inhibit or kill the cells to a greater extent than the wild-type cytotoxic protein; and (E) making copies of the selected mutant proteins, and variations thereof.

Tyrrell et al., throughout the publication, and especially at the abstract, p. 524, teach that the verotoxin, or Shiga-like toxin, family is a group of subunit toxins, with an A subunit and a B binding subunit and teach the site-directed mutagenesis of the B subunit; teach generating a library of E. coli that produced variant forms of the toxin, wherein the variant toxins include a mutation at position 18, among other targeted amino acids, as shown in fig. 1 and Table 1; wherein microorganisms were expanded and the variant toxins that each clone produces were extracted and screened in cytotoxicity assays using Vero cells, MRC-5 cells and HEp-2 tumor cells; and at p. 528, Fig. 4, teach the mutant toxin GT3 kills more HEp-2 cells than the wild-type toxin.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Jackson et al., J. of Bacteriology, Feb. 1990, Vol. 172, No. 2, pp. 653-658, (previously cited with the Requirement for Restriction/Election, mailed 8/10/04) or Tyrrell et al., Proc. Natl. Acad. Sci. USA, vol. 89, pp. 524-528, Jan 1992 (IDS filed 11/20/2000), each taken separately, and in view of Cheng et al., (US 5,869,250).

Claims 1 and 4 are drawn to the method of claim 1, wherein the library of microorganism clones producing the variant forms of heteromeric protein toxins comprises yeast or yeast supernatants.

Jackson et al., throughout the publication, and especially at the abstract, p. 653, para 1-2, and p. 655, Fig. 1, teach the Shiga and Shiga-like toxin family is a group of subunit toxins, with an A subunit and a B binding subunit, and the site-directed mutagenesis of the B subunit; at p. 653, para 3-p. 654, para 1, and p. 655, Table I, generating a library of E. coli that produced variant forms of the toxin; at p. 654, para 5-p. p. 655, para 2, teach extracellular supernatants and cell-associated fractions (of the microorganism E. coli library) that are used for microcytotoxicity assays using Vero cells and HeLa (tumor) cells and glycolipid receptor binding ELISA assays; and at para 5-p. 655, para 1, p. 656, para 4, and Table 3, teach amber termination mutations in the

Shiga toxin B unit, wherein the double suppressor host LE392 expresses 2 to 3 orders of magnitude more cytotoxicity than the single suppressor host HB101 (Table 3).

Tyrrell et al., throughout the publication, and especially at the abstract, p. 524, teach that the verotoxin, or Shiga-like toxin, family is a group of subunit toxins, with an A subunit and a B binding subunit and teach the site-directed mutagenesis of the B subunit; teach generating a library of E. coli that produced variant forms of the toxin, wherein the variant toxins include a mutation at position 18, among other targeted amino acids, as shown in fig. 1 and Table 1; wherein microorganisms were expanded and the variant toxins that each clone produces were extracted and screened in cytotoxicity assays using Vero cells, MRC-5 cells and HEp-2 tumor cells; and at p. 528, Fig. 4, teach the mutant toxin GT3 kills more HEp-2 cells than the wild-type toxin.

Jackson and Tyrrell et al., each taken separately, do not teach a library of microorganism clones producing the variant forms of heteromeric protein toxins that comprises yeast or yeast supernatants.

Cheng et al., (US 5,869,250), throughout the patent and especially at col. 4, lines 31-44, teach construction of a combinatorial library for expression in yeast.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have used a library of microorganism clones producing variant forms of heteromeric protein toxins that comprises yeast or yeast supernatants in methods for making cytotoxic mutant proteins having different receptor-binding specificity than the wild type protein.

One of ordinary skill in the art would have been motivated to use a library of microorganism clones that comprises yeast or yeast supernatants because Cheng et al. teach that yeast can express a large number of peptides from combinatorial libraries.

10. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Jackson et al., J. of Bacteriology, Feb. 1990, Vol. 172, No. 2, pp. 653-658, (previously cited with the Requirement for Restriction/Election, mailed 8/10/04) or Tyrrell et al., Proc. Natl. Acad. Sci. USA, vol. 89, pp. 524-528, Jan 1992 (IDS filed 11/20/2000), each taken separately, and in view of Reidhaar-Olson et al., Meth Enzymol (1991), vol. 208: 564-586.

Claims 1 and 6 are drawn to the method of claim 1, wherein said mutation is incorporated into said binding domain or subunit by use of a combinatorial cassette method comprising: (A) preparing synthetic mutant oliognucleotides capable of annealing with a corresponding wild type oligonucleotide from said binding domain or subunit; (B) annealing said synthetic oligonucleotide from said binding domain or subunit to an overlapping wild type oligonucleotide to form a double stranded sequence; (C) creating a combinatorial cassette by mutually primed synthesis of said double stranded sequence; and (D) incorporating said cassette into a vector containing a gene for said toxin.

Jackson et al., throughout the publication, and especially at the abstract, p. 653, para 1-2, and p. 655, Fig. 1, teach the Shiga and Shiga-like toxin family is a group of subunit toxins, with an A subunit and a B binding subunit, and the site-directed

mutagenesis of the B subunit; at p. 653, para 3-p. 654, para 1, and p. 655, Table I, generating a library of E. coli that produced variant forms of the toxin; at p. 654, para 5-p. p. 655, para 2, teach extracellular supernatants and cell-associated fractions (of the microorganism E. coli library) that are used for microcytotoxicity assays using Vero cells and HeLa (tumor) cells and glycolipid receptor binding ELISA assays; and at para 5-p. 655, para 1, p. 656, para 4, and Table 3, teach amber termination mutations in the Shiga toxin B unit, wherein the double suppressor host LE392 expresses 2 to 3 orders of magnitude more cytotoxicity than the single suppressor host HB101 (Table 3).

Tyrrell et al., throughout the publication, and especially at the abstract, p. 524, teach that the verotoxin, or Shiga-like toxin, family is a group of subunit toxins, with an A subunit and a B binding subunit and teach the site-directed mutagenesis of the B subunit; teach generating a library of E. coli that produced variant forms of the toxin, wherein the variant toxins include a mutation at position 18, among other targeted amino acids, as shown in fig. 1 and Table 1; wherein microorganisms were expanded and the variant toxins that each clone produces were extracted and screened in cytotoxicity assays using Vero cells, MRC-5 cells and HEp-2 tumor cells; and at p. 528, Fig. 4, teach the mutant toxin GT3 kills more HEp-2 cells than the wild-type toxin.

Jackson and Tyrrell et al., each taken separately, do not teach a combinatorial cassette method.

Reidhaar-Olson et al., throughout the reference, and at pp. 564-571 and 575-577, teach random mutagenesis of protein sequences using cassette mutagenesis,

including mutating a single codon to encode all naturally occurring amino acids, which reads on a combinatorial cassette method.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have used a combinatorial cassette in methods for making cytotoxic mutant proteins having different receptor-binding specificity than the wild type protein.

One of ordinary skill in the art would have been motivated to use a combinatorial cassette method in making cytotoxic mutant proteins because Reidhaar-Olson et al. teach the use of oligonucleotide cassettes to generate protein variants having random mutations.

11. Claims 1 and 7 rejected under 35 U.S.C. 103(a) as being unpatentable over either of Jackson et al., J. of Bacteriology, Feb. 1990, Vol. 172, No. 2, pp. 653-658, (previously cited with the Requirement for Restriction/Election, mailed 8/10/04) or Tyrrell et al., Proc. Natl. Acad. Sci. USA, vol. 89, pp. 524-528, Jan 1992 (IDS filed 11/20/2000), each taken separately, and in view of Nickoloff et al., (US 5,354,670).

Claims 1 and 7 are drawn to the method of claim 1 wherein said mutation is incorporated into said binding domain subunit by means of a unique site elimination method of mutageneis.

Jackson et al., throughout the publication, and especially at the abstract, p. 653, para 1-2, and p. 655, Fig. 1, teach the Shiga and Shiga-like toxin family is a group of subunit toxins, with an A subunit and a B binding subunit, and the site-directed

mutagenesis of the B subunit; at p. 653, para 3-p. 654, para 1, and p. 655, Table I, generating a library of E. coli that produced variant forms of the toxin; at p. 654, para 5-p. p. 655, para 2, teach extracellular supernatants and cell-associated fractions (of the microorganism E. coli library) that are used for microcytotoxicity assays using Vero cells and HeLa (tumor) cells and glycolipid receptor binding ELISA assays; and at para 5-p. 655, para 1, p. 656, para 4, and Table 3, teach amber termination mutations in the Shiga toxin B unit, wherein the double suppressor host LE392 expresses 2 to 3 orders of magnitude more cytotoxicity than the single suppressor host HB101 (Table 3).

Tyrrell et al., throughout the publication, and especially at the abstract, p. 524, teach that the verotoxin, or Shiga-like toxin, family is a group of subunit toxins, with an A subunit and a B binding subunit and teach the site-directed mutagenesis of the B subunit; teach generating a library of E. coli that produced variant forms of the toxin, wherein the variant toxins include a mutation at position 18, among other targeted amino acids, as shown in fig. 1 and Table 1; wherein microorganisms were expanded and the variant toxins that each clone produces were extracted and screened in cytotoxicity assays using Vero cells, MRC-5 cells and HEp-2 tumor cells; and at p. 528, Fig. 4, teach the mutant toxin GT3 kills more HEp-2 cells than the wild-type toxin.

Jackson and Tyrrell et al., each taken separately, do not teach incorporation of mutations into the binding domain subunit by a unique site elimination method.

Nickoloff et al., (US 5,354,670), et al., throughout the patent, and especially at col. 2, line 2-col. 8, line 10, teach a method of site-specific mutagenesis of DNA that can be used to mutagenize DNA, especially circular DNA, so that parental DNA, containing

nonessential, unique restriction site, is used to generate progeny DNA containing the desired mutation but lacking the restriction site.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have used unique site elimination (USE) methods for making cytotoxic mutant proteins having different receptor-binding specificity than the wild type protein.

One of ordinary skill in the art would have been motivated to use unique site elimination (USE) methods in making cytotoxic mutant proteins because Nickoloff et al. teach the use of USE methods to mutagenize DNA at particular sites.

12. Claims 1, 2, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Jackson et al., J. of Bacteriology, Feb. 1990, Vol. 172, No. 2, pp. 653-658, (previously cited with the Requirement for Restriction/Election, mailed 8/10/04) or Tyrrell et al., Proc. Natl. Acad. Sci. USA, vol. 89, pp. 524-528, Jan 1992 (IDS filed 11/20/2000), each taken separately, and in view of Frankel et al., (US 4,753,894).

The claims are drawn to the method of claim 1 wherein the screening cells are breast cancer cells and that are SK BR-3 or CAMA-I.

Jackson et al., throughout the publication, and especially at the abstract, p. 653, para 1-2, and p. 655, Fig. 1, teach the Shiga and Shiga-like toxin family is a group of subunit toxins, with an A subunit and a B binding subunit, and the site-directed mutagenesis of the B subunit; at p. 653, para 3-p. 654, para 1, and p. 655, Table I,

generating a library of E. coli that produced variant forms of the toxin; at p. 654, para 5-p. p. 655, para 2, teach extracellular supernatants and cell-associated fractions (of the microorganism E. coli library) that are used for microcytotoxicity assays using Vero cells and HeLa (tumor) cells and glycolipid receptor binding ELISA assays; and at para 5-p. 655, para 1, p. 656, para 4, and Table 3, teach amber termination mutations in the Shiga toxin B unit, wherein the double suppressor host LE392 expresses 2 to 3 orders of magnitude more cytotoxicity than the single suppressor host HB101 (Table 3).

Tyrrell et al., throughout the publication, and especially at the abstract, p. 524, teach that the verotoxin, or Shiga-like toxin, family is a group of subunit toxins, with an A subunit and a B binding subunit and teach the site-directed mutagenesis of the B subunit; teach generating a library of E. coli that produced variant forms of the toxin, wherein the variant toxins include a mutation at position 18, among other targeted amino acids, as shown in fig. 1 and Table 1; wherein microorganisms were expanded and the variant toxins that each clone produces were extracted and screened in cytotoxicity assays using Vero cells, MRC-5 cells and HEp-2 tumor cells; and at p. 528, Fig. 4, teach the mutant toxin GT3 kills more HEp-2 cells than the wild-type toxin.

Jackson and Tyrrell et al., each taken separately, do not teach screening cells that are breast cancer cells and are SK BR-3 or CAMA-I.

Frankel et al., (US 4,753,894) et al., throughout the patent, and especially at col. 3, lines 46-57, teach testing antibody conjugated to ricin toxin in cytotoxicity assays using CAMA-1 and SKBR-3 breast tumor cells.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have tested cytotoxic mutant proteins in cytotoxicity assays comprising CAMA-1 and SKBR-3 breast tumor cells.

One of ordinary skill in the art would have been motivated to screen cytotoxic mutant proteins having different receptor-binding specificity than the wild type protein because CAMA-1 and SKBR-3 breast tumor cells are an art-recognized *in vitro* model system for selecting anti-cancer agents, including those comprising a ricin protein toxin, as taught by Frankel et al.

Conclusion

13. Claims 1-16 are rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

ms

PADMASHRI PONNALURI
PRIMARY EXAMINER

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
09/601,644	12/11/00	Garvey	

EXAMINER
Shibuya

ART UNIT	PAPER
1639	11192004

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio
(<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>>, EFS Submission User Manual - ePAVE)

2. Mailed to:
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Commissioner for Patents
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Alexandria, VA 22313-1450
Arlington, Virginia 22202

3. Mailed by Federal Express, United Parcel Service or other delivery service to:
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Arlington, Virginia 22202

Mark L. Shibuya
Examiner
Art Unit: 1639

NOTICE TO COMPLY	Application/Control No.	Applicant(s)	
	09/601,644	Gariepy	
	Examiner	Art Unit	
	Shibuya	1639	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☑ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☑ 7. Other: . The Sequence Listing is incomplete, Please see Office action mailed herewith.

Applicant Must Provide:

☑ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☑ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☑ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
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